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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/701,394 | 01/17/2001 | Glenn Nardone | 079498/0146 | 8153 |

22428 7590 05/09/2003

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER

CHUNDURU, SURYAPRABHA

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
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1637

DATE MAILED: 05/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/701,394

Applicant(s)

NARDONE, GLENN

Examiner

Suryaprabha Chunduru

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-74 is/are pending in the application.
- 4a) Of the above claim(s) 26-74 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 22 and 23 is/are allowed.
- 6) ☒ Claim(s) 1-21, 24 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-25) in Paper No. 10 is acknowledged. The traversal is on the ground(s) that there is no undue burden upon examiner to examine all the claims in the two Groups. This is not found persuasive because burden of search is not a requirement for the lack of unity. Thus the restriction requirement is still deemed proper.
2. Claims 1-25 in Group I will be considered in this office action for examination. Claims 26-74 are withdrawn from further consideration.

Priority

3. This instant Application is a 371 of PCT/US99/12799 filed on June 6, 1999 and claims benefit of a provisional application No. 60/089, 119 filed on June 12, 1998.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A. Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant Claim 1 is indefinite over the recitation of "capable of emitting" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited donor moiety have the potential to emit a quantum energy or do in fact do emit quantum energy. Amendment of the claim to read, for example, "which emits" would obviate this rejection.

B. The term "substantial" in claim 1 and its dependent claims 2-25 is a relative term, which renders the claim indefinite. The term "substantial" is not defined by the claim, the

Art Unit: 1637

specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention because the claim does not recite what amount is equal to substantial amount which can prevent a hairpin formation / or facilitate hairpin formation.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-21, and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nazarenko et al. (USPN. 5,866,336) in view of Heller (5, 532,129).

With reference to the instant claim 1-3, Nazarenko et al. teach an oligonucleotide containing (a) first nucleotide (see column 57, lines 29-32); (b) a second nucleotide sequence at the 5' end of the first nucleotide sequence (see column 57, lines 33-34); (c) a third nucleotide sequence at the end of the second nucleotide sequence (see column 57, lines 35-36); (d) a molecular energy transfer including an energy donor moiety and an energy acceptor moiety (see column 57, lines 37-50, column 19, lines 42-67) wherein energy donor moiety emits a quantum of energy and the acceptor moiety absorbs the quantum of energy, and the moieties can be located on either terminal nucleotides at 5' end or internally located nucleotides (see column 20, lines 52-65), and donor-acceptor FRET pair could be located on the same oligonucleotide sequence and double labeling of the FRET pairs on each nucleotide sequence increases the separation between the excitation and the emission frequencies of a label and thereby decreases

background fluorescence signal (see column 23, lines 12-22). Nazarenko et al. also teach said oligonucleotide forms a hairpin structure depending upon the quenching of quantum energy by acceptor moiety (see column 9, lines 21-43, column 13, lines 15-22, column 21, lines 1-23, column 22, lines 59-65).

With reference to the instant claims 4-8, Nazarenko et al. also teach that the oligonucleotide could be a DNA or RNA or chimeric mixture (see column 16, lines 3-4); said oligonucleotide further comprises a fourth nucleotide sequence which is not complementary to the third nucleotide sequence, at the end of the first nucleotide sequence (see column 57, lines 37-40) and is complementary to second nucleotide sequence which flank a target DNA sequence (see column 12, lines 1-11, column 57, lines 37-40).

With reference to the instant claims 9-21, Nazarenko et al. further teach that said oligonucleotide contains a donor and acceptor as fluorophores emitting quantum energy (see column 18, lines 29-42); ROX and DABCYL as an acceptor moiety (see column 18, lines 29-42, column 23, lines 3-6); the donor-acceptor moieties could be attached 5bp or 25 nucleotides apart or less than 1 nucleotide apart in the said oligonucleotide (see column 20, lines 66-67, column 21, lines 1-23, column 22, lines 59-65).

With reference to the instant claims 24-25, Nazarenko et al. also teach a kit comprising the said oligonucleotide and DNA polymerase (see column 32, lines 21-39, column 58, lines 30-48, column 59, lines 24-60).

However Nazarenko et al. specifically did not teach second acceptor molecule of the oligonucleotide.

Heller teaches chromophore containing polynucleotides having multiple donor chromophores and an acceptor (see column 4, lines 6-15) and a quencher positioned between a donor and an acceptor facilitates the quenching emission from the acceptor molecule (see column 4, lines 59-65). Heller also teaches that multiple donor system comprising non-fluorescing donors are valuable in reducing signal-noise-ratio (see column 7, lines 45-62); and Heller also teaches that under some conditions for certain photonic mechanisms more than one acceptor group may be used (see column 8, lines 46-61).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to combine a composition of an oligonucleotide as taught by Nazarenko et al. with the teachings as taught by Heller to achieve expected advantage of developing a sensitive and specific oligonucleotide composition for the expected advantage of developing an oligonucleotide containing more than one acceptor molecule because Heller suggests that "there are special arrangements in which certain chromophore groups with strong quenching properties are used to prevent fluorescent emission by the acceptor. The quencher chromophore having the capacity to accept, like an acceptor and does not have significant emission is referred to as non-fluorescing donor (see column 9, lines 14-25). An ordinary practitioner would have been motivated to combine the teaching of Nazarenko et al. with the teachings of Heller to improve the sensitivity and specificity of the said oligonucleotide by incorporating the second acceptor because this limitation would reduce signal-noise ratio, which would result in an efficient composition of the oligonucleotide.

Conclusion

Claims 22-23 are free of prior art and are allowable.


Art Unit: 1637

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


Suryaprabha Chunduru
April 23, 2003


JEFFREY FREDMAN
PRIMARY EXAMINER